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NEWS 8 Mar 22 TRCTHERMO no longer available
NEWS 9 Mar 28 US Provisional Priorities searched with P in CA/CAPLUS and USPATFULL
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NEWS 16 Apr 22 Records from IP.com available in CAPLUS, HCAPLUS, and ZCAPLUS
NEWS 17 Apr 22 BIOSIS Gene Names now available in TOXCENTER
NEWS 18 Apr 22 Federal Research in Progress (FEDRIP) now available
NEWS 19 May 31 PCTFULL to be reloaded. File temporarily unavailable.

NEWS EXPRESS February 1 CURRENT WINDOWS VERSION IS V6.0d,
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FILE 'BIOSIS' ENTERED AT 07:13:57 ON 03 JUN 2002
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=> s zauderer M?/au
L1 127 ZAUDERER M?/AU

=> s l1 and ct1?
L2 4 L1 AND CTL?

=> dup rem 12
PROCESSING COMPLETED FOR L2
L3 4 DUP REM L2 (0 DUPLICATES REMOVED)

=> dis l3 1-4 ibib abs

L3 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002123514 CAPLUS
DOCUMENT NUMBER: 136:182454
TITLE: Methods for identifying and producing antigens for
treating cancer and infection
INVENTOR(S): Zauderer, Maurice
PATENT ASSIGNEE(S): University of Rochester, USA
SOURCE: U.S. Pat. Appl. Publ., 54 pp., Division of U.S. Ser.
No. 935,377.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002018785	A1	20020214	US 2001-822250	20010402

PRIORITY APPLN. INFO.: US 1997-935377 A3 19970922
AB The present invention relates to novel methods for the identification of
antigens recognized by cytotoxic T cells (CTLs) and specific for
human tumors, cancers, and infected cells, and the use of such antigens in
immunogenic compns. or vaccines to induce regression of tumors, cancers,

or infections in mammals, including humans. The invention encompasses methods for induction and isolation of cytotoxic T cells specific for human tumors, cancers and infected cells, and for improved selection of genes that encode the target antigens recognized by these specific T cells. The invention also relates to differential display methods that improve resoln. of, and that reduce the frequency of false positives of DNA fragments that are differentially expressed in tumorous, cancerous, or infected tissues vs. normal tissues. The invention further relates to the engineering of recombinant viruses as expression vectors for tumor, cancer, or infected cell-specific antigens.

L3 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:780722 CAPLUS

DOCUMENT NUMBER: 135:348863

TITLE: Targeted vaccine delivery systems

INVENTOR(S): Zauderer, Maurice; Smith, Ernest S.

PATENT ASSIGNEE(S): University of Rochester, USA

SOURCE: PCT Int. Appl., 167 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001078768	A2	20011025	WO 2001-US11912	20010412
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.: US 2000-196472P P 20000412

AB The present invention is directed to a novel targeted vaccine delivery system, comprising one or more MHC-peptide complexes linked to an antibody which is specific for a cell surface marker. The complexes of the invention are useful for treating and/or preventing cancer, infectious diseases, autoimmune diseases, and/or allergies.

L3 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:747830 CAPLUS

DOCUMENT NUMBER: 135:314437

TITLE: Identification and characterization of a novel gene C35 differentially expressed in breast and bladder cancer and cancer immunotherapy thereof

INVENTOR(S): Zauderer, Maurice; Evans, Elizabeth E.; Borrello, Melinda A.

PATENT ASSIGNEE(S): University of Rochester, USA

SOURCE: PCT Int. Appl., 331 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001074859	A2	20011011	WO 2001-US10855	20010404
WO 2001074859	A3	20020328		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2000-194463P P 20000404

AB The present invention relates to a novel human gene that is differentially expressed in human carcinoma. More specifically, the present invention relates to a polynucleotide encoding a novel human polypeptide named C35 that is overexpressed in human breast and bladder carcinoma. The full-length gene aligns on human chromosome 17q12 and mouse chromosome 11 and encodes a novel 115 amino acid membrane protein of unknown function. A monoclonal antibody, 2C3, has been selected which can detect the C35 surface expression by flow cytometric anal. and is shown to inhibit the growth of C35 overexpressed tumor cell lines. In addn., human cytotoxic T lymphocytes (CTL) have been generated in vitro that specifically lyse C35+ breast and bladder tumors. These T cells are strongly stimulated to secrete interferon .alpha. and interferon .gamma. by the breast lines that expressed both C35 and HLA-A2, indicate that there is at least one C35 Class I epitope is HLA-A2 restricted. Overexpression of C35 in tumors of different individuals and the ability to induce humoral and cellular immune responses make C35 a promising candidate for immunotherapy.

L3 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:335539 CAPLUS

DOCUMENT NUMBER: 133:1478

TITLE: Methods for identifying genes of tumor specific antigens recognized by cytotoxic T cells and cancer vaccines based thereon

INVENTOR(S): Zauderer, Maurice

PATENT ASSIGNEE(S): University of Rochester, USA

SOURCE: PCT Int. Appl., 132 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000028016	A1	20000518	WO 1998-US24029	19980110

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX,

NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT,
 UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
 RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES,
 FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,
 CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
 AU 9913977 A1 20000529 AU 1999-13977 19981110
 EP 1137769 A1 20011004 EP 1998-957808 19981110
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, FI
 PRIORITY APPLN. INFO.: WO 1998-US24029 A 19981110
 AB The present invention relates to novel methods for the identification of genes of antigens recognized by cytotoxic T cells (CTLs) and specific for human tumors, cancers, and infected cells, and the use of genes of such antigens in immunogenic compns. or vaccines to induce regression of tumors, cancers, or infections in mammals, including humans. The invention also relates to differential display methods that improve resoln. of, and that reduce the frequency of false positives of DNA fragments that are differentially expressed in tumorous, cancerous, or infected tissues vs. normal tissues. The invention further relates to the engineering of recombinant viruses as expression vectors for tumor, cancer, or infected cell-specific antigens.
 REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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=> s librar?
L4      192122 LIBRAR?  

=> s l4 (P) CTL
L5      366 L4 (P) CTL  

=> s PD <19970922
'19970922' NOT A VALID FIELD CODE
SYSTEM LIMITS EXCEEDED - SEARCH ENDED
75% OF LIMIT FOR TOTAL ANSWERS REACHED
3 FILES SEARCHED...
SYSTEM LIMITS EXCEEDED - SEARCH ENDED
The search profile you entered was too complex or gave too many answers. Simplify or subdivide the query and try again. If you have exceeded the answer limit, enter DELETE HISTORY at an arrow prompt (>) to remove all previous answers sets and begin at L1. Use the SAVE command to store any important profiles or answer sets before using DELETE HISTORY.
  
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=> s PD<19970922
'19970922' NOT A VALID FIELD CODE
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u
SEARCH ENDED BY USER
The search profile you entered was too complex or gave too many answers. Simplify or subdivide the query and try again. If you have exceeded the answer limit, enter DELETE HISTORY at an arrow prompt (>) to remove all previous answers sets and begin at L1. Use the SAVE command to store any important profiles or answer sets before using DELETE HISTORY.
  
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=> s l5 and PD<19970922
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3 FILES SEARCHED...
L6      146 L5 AND PD<19970922  

=> s l6 (P) (epitop? or peptid?)
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L22 (P)'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L23 (P)'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L24 (P)'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L25 (P)'
L7      89 L6 (P) (EPITOP? OR PEPTID?)  

=> dis his
  
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(FILE 'HOME' ENTERED AT 07:13:43 ON 03 JUN 2002)

FILE 'MEDLINE, CAPLUS, EMBASE, BIOSIS' ENTERED AT 07:13:57 ON 03 JUN 2002
L1      127 S ZAUDERER M7/AU
L2      4 S L1 AND CTL?
L3      4 DUP REM L2 (0 DUPLICATES REMOVED)
L4      192122 S LIBRAR?  

L5      366 S L4 (P) CTL
L6      146 S L5 AND PD<19970922
L7      89 S L6 (P) (EPITOP? OR PEPTID?)  

  
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=> s l7 and mhc
L8      39 L7 AND MHC  

=> dis 18 1-39 ibib abs
  
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L8	ANSWER 1 OF 39	CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER:	1997:462415	CAPLUS
DOCUMENT NUMBER:	127:189254	
TITLE:	Antigen processing by proteasomes: insights into the molecular basis of crypticity	
AUTHOR(S):	Djaballah, Hakim	
CORPORATE SOURCE:	MRC Transplantation Biology Group, Royal Postgraduate Medical School, Hammersmith Hospital, London, W12 0NN, UK	
SOURCE:	Mol. Biol. Rep. (1997), 24(1-2), 63-67	
PUBLISHER:	Kluwer	
DOCUMENT TYPE:	Journal, General Review	
LANGUAGE:	English	

AB A review with 44 refs. Eight to eleven amino acid residues are the sizes of predominant peptides found to be assoccd. with MHC class I molc. Proteasomes have been implicated in antigen processing and generation of such peptides. Advanced methodologies in peptide elution together with sequence detn. have led to the characterization of MHC class I binding motifs. More recently, screening of random peptide phage display libraries and synthetic combinatorial peptide libraries have

also been successfully used. This has led to the development and use of predictive algorithms to screen antigens for potential cytotoxic T-lymphocyte (CTL) epitopes. Not all predicted epitopes will be generated in vivo and the emerging picture suggests differential presentation of predicted CTL epitopes ranging from cryptic to immunodominant. Antigen processing by proteasomes is discussed, a hypothesis that the mol. basis of immunogenicity can be a function of proteasomal processing is advanced. This may explain how pathogens and tumors are able to escape immunosurveillance by altering sequences required by proteasomes for epitope generation.

L8 ANSWER 2 OF 39 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:147340 CAPLUS
DOCUMENT NUMBER: 126:198410
TITLE: Cytotoxic T cell induction with ratchet peptide libraries
AUTHOR(S): Kuebler, Peter J.; Nixon, Douglas F.
CORPORATE SOURCE: United Biomedical, Inc., Hauppauge, NY, 11788, USA
SOURCE: Vaccine (1996), 14(17/18), 1664-1670
CODEN: VACCDE; ISSN: 0264-410X
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Immunization with synthetic peptides are used to induce cytotoxic T cell (CTL) responses in vivo. However, CTL peptide vaccines require the use of multiple peptides to overcome genetic diversity assoc'd. with MHC restriction, and prior epitope identification from the chosen protein template. The authors describe here a method whereby all nonamer sequences from a longer template can be synthesized simultaneously in a ratchet peptide library (RPL) covering all potential epitopes within a protein. The authors synthesized an RPL based on a template sequence from the Plasmodium berghei circumsporozoite (CS) protein (CSRPL). Using a lipopeptide formulation the authors immunized mice i.p. with the CSRPL and elicited CS specific CTL, which recognized the CS252-260 H-2Kd restricted CTL epitope.

L8 ANSWER 3 OF 39 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:111450 CAPLUS
DOCUMENT NUMBER: 126:184804
TITLE: Identification of tyrosinase-related protein 2 as a tumor rejection antigen for the B16 melanoma
AUTHOR(S): bloom, Matthew b.; Perry-Lalley, Donna; Robbins, Paul F.; Li, Yong; El-Gamil, Mona; Rosenberg, Steven A.; Yang, James C.
CORPORATE SOURCE: Natl. Cancer Inst., Natl. Inst. Health, Bethesda, MD, 20892, USA
SOURCE: J. Exp. Med. (1997), 185(3), 453-459
CODEN: JEMEAV; ISSN: 0022-1007
PUBLISHER: Rockefeller University Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Recently, major advances have been made in the identification of antigens from human melanoma which are recognized by T cells. In spite of this, little is known about the optimal ways to use these antigens to treat patients with cancer. Progress in this area is likely to require accurate preclin. animal models, but the availability of such models has lagged behind developments in human tumor immunol. Whereas many of the identified human melanoma antigens are normal tissue differentiation proteins, analogous murine tumor antigens have not yet been identified. In this paper we identify normal tissue differentiation antigen, tyrosinase-related protein 2 (TRP-2), expressed by the murine B16 melanoma which was found by screening a cDNA library from B16 with tumor-reactive cytotoxic T lymphocytes (CTL). A peptide conforming to the predicted MHC class I H2-K^b binding motif, TRP-2-2181-188, was identified a the major reactive epitope within TRP-2 recognized by these anti-B16 CTLs. By site-directed mutagenesis, it was shown that alteration of this epitope eliminated recognition of TRP-2. It was further demonstrated that the CTL line obtained from splenocytes by repeated stimulation in vitro with this peptide could recognize B16 tumor and was therapeutic against 3-d-old established pulmonary metastases. The use of TRP-2 in a preclin. model of tumor immunotherapy may be helpful in suggesting optimal vaccination strategies for cancer therapy in patients.

L8 ANSWER 4 OF 39 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:72877 CAPLUS
DOCUMENT NUMBER: 126:143035
TITLE: Identification of potential CTL epitopes of bovine RSV using allele-specific peptide motifs from bovine MHC class I molecules
AUTHOR(S): Gaddum, R. M.; Ellis, S. A.; Willis, A. C.; Cook, R. S.; Staines, K. A.; Thomas, L. H.; Taylor, G.
CORPORATE SOURCE: Inst. Animal Health, Compton, Newbury, RG20 7NN, UK
SOURCE: Vet. Immunol. Immunopathol. (1996), 54(1-4), 211-219
CODEN: VIIMDS; ISSN: 0165-2427
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Respiratory syncytial virus (RSV) is a major cause of lower respiratory tract infection in young infants and housed calves. Depletion of CD8⁺ lymphocytes from calves inhibited their ability to clear the virus from the nasopharynx and lungs. To study these cells further, a cytotoxic T lymphocyte (CTL) assay was established. CTL could be demonstrated in the peripheral blood of gnotobiotic calves 7-10 days post infection (p.i.) with RSV and in lungs 10 days p.i. This response was both MHC-restricted and virus-specific. Following sepn. of the lung lymphocytes by magnetic activated cell sorting, it was shown that the cytolytic activity was mediated by cells of the CD8⁺ phenotype. To identify epitopes recognized by bovine CTL, the consensus motifs from MHC class I alleles were identified. cDNA libraries were constructed and screened for full length class I sequences. The isolated cDNA clones were then transfected into mouse P815 cells and the expressed product immunopptd. and matched with a serol. specificity. The bovine MHC class I mols. were isolated from lysed transfected cells by affinity chromatog., using a monoclonal antibody specific for bovine MHC class I, and bound peptides were sep'd. by reverse-phase HPLC. Anal. of the protein sequences of bovine RSV for the defined motifs has identified potential CTL epitopes.

L8 ANSWER 5 OF 39 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1996:563443 CAPLUS
 DOCUMENT NUMBER: 125:219603
 TITLE: Peptide ratchet libraries for
 CTL-inducing vaccines and therapeutics
 INVENTOR(S): Kuebler, Peter J.; Nixon, Douglas F.
 PATENT ASSIGNEE(S): United Biomedical, Inc., USA
 SOURCE: PCT Int. Appl., 60 pp.
 CODEN: PIXKD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9622067	A2	19960725	WO 1995-US16290	19951215 <-
WO 9622067	A3	19961128		
W: AU, CA, FI, JP, NO RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE AU 9658497	A1	19960807	AU 1996-58497	19951215 <-
PRIORITY APPLN. INFO.:			US 1994-366332	19941227
			WO 1995-US16290	19951215

AB The present invention relates to ratchet libraries composed of related peptides synthesized simultaneously in a single peptide synthesis. Ratchet libraries are derived from a longer template peptide by sequentially "ratcheting" the template sequence into the shorter ratchet length and are used for cytotoxic T lymphocyte (CTL) induction or stimulation if the CTL epitope is known. If the CTL epitope is unknown, then the ratchet library can be used for identification of CTL epitopes. The ratchet libraries can be prep'd. from any protein sequence to which an immune CTL response is desired and can be formulated for delivery as a vaccine or therapeutic for the treatment or prevention of disease or malignancy. For example, a ratchet library can be used in the prevention and treatment of infectious or malignant diseases including HIV, influenza, malaria, breast, ovarian, lung and colon cancers.

L8 ANSWER 6 OF 39 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1996:422019 CAPLUS
 DOCUMENT NUMBER: 125:84043
 TITLE: Use of combinatorial peptide libraries to construct functional mimics of tumor epitopes recognized by MHC class I-restricted cytolytic T lymphocytes
 AUTHOR(S): Blake, James; Johnston, Janet V.; Hellstroem, Karl Erik; Marquardt, Hans; Chen, Lieping
 CORPORATE SOURCE: Bristol-Myers Squibb Pharmaceutical Res. Inst., Seattle, WA, 98121, USA
 SOURCE: J. Exp. Med. (1996), 184(1), 121-130
 CODEN: JEMEAV; ISSN: 0022-1007
 DOCUMENT TYPE: Journal
 LANGUAGE: English

AB Identification of cytolytic T lymphocyte (CTL) epitopes presented by major histocompatibility complex (MHC) class I mol's. on tumor cells is crit. for the design of active immunotherapy. We describe the use of combinatorial peptide libraries with defined amino acids in two MHC anchor positions to search for epitopes that are recognized by H-2Db- and Kb-restricted CTL specific for the mouse lymphoma EL4. An iterative strategy was used for screening libraries in which 16 amino acids were divided into 3 groups and 3 subgroups: .alpha.(AL, VT, FY); .beta.(GS, P, DE); .gamma.(KR, H, NQ). The proportions of each group and subgroup at individual peptide positions were changed in the library synthesis, and the effect of these changes on CTL activity was measured in a sensitive RMA-S cell assay. A single H-2Db epitope mimic was deduced from the original library that contained >2 times 108 potential peptides and was at least 9 logs more potent than the original library. Immunization of syngeneic mice with this peptide elicited CTL that lysed EL4 cells as well as RMA-S cells pulsed with peptides isolated from Db mol's. of EL4 cells, indicating functional similarity between the mimicking peptide and the naturally processed CTL epitope. Furthermore, adoptive transfer of such a CTL line had a therapeutic effect in mice with EL4 established as an ascites tumor. Two H-2Kb-restricted epitope mimics of the same tumor were also identified. Our method represents a novel approach for the construction of MHC class I-restricted targets that can serve as immunogens for active immunotherapy of cancer.

L8 ANSWER 7 OF 39 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1996:408481 CAPLUS
 DOCUMENT NUMBER: 125:84015
 TITLE: Self-MHC-restricted peptides

AUTHOR(S): Ueda, Keiko; Wiesmueller, Karl-Heinz; Kienle, Stefan; Jung, Guenther; Walden, Peter
 CORPORATE SOURCE: Max Planck Inst. Biology, Immunogenetics Section, Tuebingen, Germany
 SOURCE: J. Immunol. (1996), 157(2), 670-678
 CODEN: JOIMAS; ISSN: 0022-1767
 DOCUMENT TYPE: Journal
 LANGUAGE: English

AB Alloreactive T lymphocytes are readily detected in unprimed animals although they have never encountered the alloantigen before. This well-established phenomenon is usually explained with the assumption that a self-MHC mol. complexed with a defined peptide resembles the allo-MHC mol. with another peptide and induces the corresponding T cell specificities. Here, for the first time and in support of this hypothesis, self-MHC-restricted peptides are described for a T cell clone that was induced with allo-MHC. The allo-MHC-specific CTL clone 2C was derived from a H-2b mouse and recognizes H-2Ld complexed with the naturally occurring endogenous peptide LSPFPDYL. H-2Kb was shown to be involved in pos. selection of its TCR, and peptides assoc'd. with this MHC mol. are implicated in the process. To identify such peptides, positional scanning with random peptide libraries combined with an iterative approach was employed. Several active peptides were found and the most

efficient, SIYRYYGL, was chosen for further studies. Recognition by 2C of the two MHC-peptide adducts H-2Ld + LSPPPFDL and H-2Kb + SIYRYYGL is mediated by the same TCR and appears to be similarly efficient as concluded from inhibition expts. with an Id-specific Ab. CTLs from SIYRYYGL-primed H-2b mice respond to H-2Ld + LSPPPFDL. This reciprocal cross-reactivity suggests that structural features are shared by the two MHC-peptide complexes.

L8 ANSWER 8 OF 39 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:282493 CAPLUS
DOCUMENT NUMBER: 124:340313
TITLE: Specificity and degeneracy of minor histocompatibility antigen-specific MHC-restricted CTL
AUTHOR(S): Gundlach, Bjoern R.; Wiesmueller, Karl-Heinz; Junt, Tobias; Kienle, Stefan; Jung, Guenther; Walden, Peter
CORPORATE SOURCE: Section Immunogenet., Max Planck Inst. Biol., Tuebingen, Germany
SOURCE: J. Immunol. (1996), 156(10), 3645-3651
CODEN: JOIMA3; ISSN: 0022-1767
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Random peptide libraries were employed to investigate the specificity of Ag recognition by H-3-specific, H-2Kb-restricted CTL clones. The peptide libraries consist of octapeptides with one defined sequence position and mixts. of 19 amino acids (all proteinogenic amino acids except for cysteine) in the remaining seven sequence positions. The complete set of 152 peptide libraries includes all octapeptides possible with these amino acids. Responses of the CTL clones to these peptide libraries reveal patterns of preferred epitope amino acids. Depending on the CTL clone tested, varying nos. of different amino acids were identified for the different sequence positions indicating degeneracy of Ag recognition. Sequences for synthetic epitopes active at low pM concns. could be deduced from these patterns. They confirm that TCRs of CTL clones do not exhibit specificity for unique ligand structures but rather can interact with sets of ligands. The sequences of peptides recognized by a single clone exhibit great sequence heterogeneity.

L8 ANSWER 9 OF 39 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:11929 CAPLUS
DOCUMENT NUMBER: 124:53176
TITLE: Increased peptide promiscuity provides a rationale for the lack of N regions in the neonatal T cell repertoire
AUTHOR(S): Gavin, Marc A.; Bevan, Michael J.
CORPORATE SOURCE: Dept. Immunology, Univ. Washington, Seattle, WA, 98195-7370, USA
SOURCE: Immunity (1995), 3(6), 793-800
CODEN: IUNIEH; ISSN: 1074-7613
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Making use of mice deficient for terminal deoxynucleotidyl transferase (TdT) expression and a random peptide library, the authors have exmd. the diversity and peptide specificity of the neonatal T cell repertoire specific for a single H-2Db-restricted peptide. Consistent with the predicted decrease in repertoire diversity, polyclonal CTL lines and individual clones from different TdT^{-/-} mice are more similar to each other than those from different wild-type mice in terms of their fingerprints of cross-reactivity to the library and their TCR sequences. Also, several TdT^{-/-} CTL clones cross-react with many more library peptides than wild-type CTL clones. In a few instances, the degree of peptide promiscuity correlates with TCR sequence characteristics such as N region addn. and homol.-directed recombination, but not CDR3 loop length. Based on epitope titrns. for each clone, TCR affinity for antigen is consistently high; thus, this reduced specificity for peptide may coincide with an accentuated affinity for the .alpha. helixes of the MHC. Peptide promiscuity in the neonate may allow the relatively small nos. of T cells in the periphery to protect against a broader range of pathogens.

L8 ANSWER 10 OF 39 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:590067 CAPLUS
DOCUMENT NUMBER: 123:53835
TITLE: Decrpting the structure of major histocompatibility complex class I-restricted cytotoxic T lymphocyte epitopes with complex peptide libraries
AUTHOR(S): Ueda, Keiko; Wiesmueller, Karl-Heniz; Kienle, Stefan; Jung, Guenther; Walden, Peter
CORPORATE SOURCE: Max-Planck-Institut Biologie, Tuebingen, D-72076, Germany
SOURCE: J. Exp. Med. (1995), 181(6), 2097-108
CODEN: JEMEAV; ISSN: 0022-1007
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Complex synthetic peptide libraries with defined amino acids in one or more positions of the H-2Kb-restricted cytotoxic T lymphocyte (CTL) epitopes SIINFEKL and RGVYYQQL and mixts. of 19 amino acids in the remaining positions were used to analyze the structural requirements of peptide binding to MHC class I mols. and antigen recognition by CTLs. This approach provides means to assess semiquant. the contribution of every amino acid to the binding of peptides to major histocompatibility complex (MHC) mols. without biases introduced by naturally processed peptides. Primary and secondary anchor residues were defined for their major contribution to the binding efficiency of the peptides. In contrast to primary anchors, secondary anchor amino acids vary greatly in their side chains and position in the sequences. All amino acids in the octapeptide sequences were found to exhibit pos. or neg. influences on binding to the MHC mols. and on recognition of the resulting complexes by CTLs. Strong interdependence of the effects of the individual residues in the epitope sequences was demonstrated. CTL responses to peptide libraries were suppressed when residues were introduced; however, they were augmented when the crit. residues of T cell recognition were fixed, suggesting a potential use of the peptide libraries for defining epitope sequences in general.

L8 ANSWER 11 OF 39 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1995:497868 CAPLUS
DOCUMENT NUMBER: 122:263117
TITLE: Isolation of a kidney-specific peptide
recognized by alloreactive HLA-A3-restricted human CTL
AUTHOR(S): Poindexter, Nancy J.; Naziruddin, Bashoo; McCourt,
David W.; Mohanakumar, T.
CORPORATE SOURCE: Dep. Surg., Howard Hughes Med. Inst., St. Louis, MO,
63110, USA
SOURCE: J. Immunol. (1995), 154(8), 3880-7
CODEN: JOIMAA; ISSN: 0022-1767
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The mol. nature of tissue-specific Ags involved in MHC-restricted CTL responses is as yet undefined. To det. the specificity of these peptides, their function, and their possible relationship to allograft rejection, we have utilized human kidney-specific CD8+ CTL clones to screen reversed-phase HPLC (RP-HPLC)-sepd. self peptides presented by allo-class I mole. One of these clones is HLA-A3-restricted and the other HLA-B62-restricted, lysing human kidney cell lines but not MHC identical B lymphoblastoid cells which express the appropriate HLA mole. We have identified the biol. active RP-HPLC fraction contg. self peptides eluted from affinity-purified MHC mole. from HLA-A3+ kidney. This peptide is not expressed in HLA-A3+ spleen. Similarly, a HLA-B62-assoccd. peptide fraction was identified in kidney but not in spleen using the HLA-B62-restricted CTL clone. Sequence anal. of the biol. active fraction from HLA-A3 kidney revealed multiple peptides. Because of the ambiguity of the peptide sequence, a mixed peptide library corresponding to this sequence was synthesized that included the HLA-A3 binding motif. The biol. active peptide library was RP-HPLC fractionated and the fraction contg. HLA-A3-restricted CTL activity was sequenced. The resulting sequence of the alloreactive HLA-A3-restricted peptide epitope is GPPGVITVK. By using this unique strategy, we describe the successful isolation and sequencing of an antigenic peptide that is recognized by a human alloreactive kidney-specific CTL clone.

L8 ANSWER 12 OF 39 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1994:28784 CAPLUS
DOCUMENT NUMBER: 120:28784
TITLE: Peptide presentation by major histocompatibility complex-class I and in vivo induction of cytotoxic T-lymphocytes
AUTHOR(S): Jung, Guenther
CORPORATE SOURCE: Inst. Org. Chem., Eberhard-Karls-Univ., Tuebingen, D-7400, Germany
SOURCE: Pept. Chem. 1992, Proc. Jpn. Symp., 2nd (1993***)
, Meeting Date 1992, 627-31. Editor(s): Yanaihara, Noboru. ESCOM: Leiden, Neth.
CODEN: 59NTAC
DOCUMENT TYPE: Conference; General Review
LANGUAGE: English

AB A review with 23 refs. on the development of novel methods for sequencing the self- ***peptide pools isolated from MHC-I mols., which the authors call natural peptide libraries. These anal. methods are based on automated Edman degdgn. and electrospray-MS of peptide mixts. The sequence motifs of the self-peptide mixts. (natural peptide libraries), isolated from several MHC-I alleles and pool sequenced, allow the exact prediction of CTL epitopes. Therefore, minimal lipopeptide vaccines for in vivo elicitation of allele-specific CTL immune response can be constructed.

L8 ANSWER 13 OF 39 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1992:589973 CAPLUS
DOCUMENT NUMBER: 117:189973
TITLE: Influenza basic polymerase 2 peptides are recognized by influenza nucleoprotein-specific cytotoxic T lymphocytes
AUTHOR(S): Anderson, Robert W.; Bennink, Jack R.; Yewdell, Jonathan W.; Maloy, W. Lee; Coligan, John E.
CORPORATE SOURCE: Biol. Resour. Branch, Natl. Inst. Allergy Infect. Dis., Bethesda, MD, 20892, USA
SOURCE: Mol. Immunol. (1992), 29(9), 1089-96
CODEN: MOIMD5; ISSN: 0161-5890
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Cytotoxic T lymphocytes (CTL) play an important role in limiting viral infections and in eradicating virus from host tissues. Recent progress in understanding the processing and presentation of viral antigens to CTL indicates that the CTL antigen receptor recognizes peptides derived from viral proteins that are bound to an antigen binding groove present in class I major histocompatibility complex (MHC) mols. In understanding CTL anti-viral responses and in creating vaccines designed to elicit CTL responses, it is crit. to identify the portions of viral proteins that bind class I mols. and are recognized by T cell receptors. Previous findings have indicated that a significant portion of the CTL response of H-2d mice to influenza virus is specific for one of the viral polymerases (PB2). To identify the region of PB2 naturally processed and presented by influenza virus-infected mouse cells to CTL, 31 PB2 peptides of 9-16 residues in length were chosen and chem. synthesized. Two peptides, PB2 residues 146-159 and 187-195, sensitized histocompatible target cells for recognition by influenza virus-specific CTL. When CTL were generated to individual viral proteins using influenza-vaccinia recombinant viruses, PB2-specific CTL failed to recognize cells sensitized with PB2 peptides 146-159 and 187-195. Further anal. showed that these PB2 peptides were, in fact, recognized by nucleoprotein (NP)-specific CTL generated by recombinant NP-vac virus priming and influenza A virus stimulation, or NP peptide stimulation in vitro of NP-vac or influenza A-primed CTL. Thus, while screening peptide libraries one cannot assume that pos. peptides necessarily identify the viral protein to which the CTL response is directed.

L8 ANSWER 14 OF 39 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1991:629907 CAPLUS
DOCUMENT NUMBER: 115:229907
TITLE: A single amino acid substitution in an MHC class I molecule allows heteroclitic recognition by

lymphocytic choriomeningitis virus-specific cytotoxic
 T lymphocytes
AUTHOR(S): Muller, Daniel; Pederson, Katrina; Murray, Richard;
CORPORATE SOURCE: Dep. Microbiol. Immunol., Univ. North Carolina, Chapel Hill, NC, 27599-7290, USA
SOURCE: J. Immunol. (1991), 147(4), 1392-7
CODEN: JOIMAS; ISSN: 0022-1767
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Class I mol. of the MHC bind foreign and endogenous peptides allowing recognition by the TCR on CTL. The recognition and killing of cells infected with lymphocytic choriomeningitis virus (LCMV) depends on the recognition of LCMV peptides bound to class I MHC. Mutations in class I MHC mol. have enabled the delineation of regions in the class I mol. important for binding peptides and for interaction with the TCR. A library of class I mutants was constructed using satn. mutagenesis and a phenotypic change resulting from a single amino acid substitution is reported that results in the heteroclitic (increased) killing of LCMV-infected cells. This amino acid change, asparagine to serine at position 30, is in a conserved region of the class I mol. contacting the .alpha.3 domain. This mutation does not result in increased expression of the class I mol. on the cell surface, does not affect the binding of CD8, and does not affect allogeneic recognition. Cold target expts. show that this heteroclitic killing is due to increased recognition by CTL. These data point toward a crit. function for this region of the class I mol. in the binding of peptides or their presentation to CTL.

L8 ANSWER 15 OF 39 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1989:2041 CAPLUS
DOCUMENT NUMBER: 110:2041
TITLE: The murine MHC class I genes, H-2D^a and H-2L^a, are strikingly homologous to each other, H-2D^b, and two genes reported to encode tumor-specific antigens
AUTHOR(S): Lee, David R.; Rubocki, Ronald J.; Lie, Wen Rong; Hansen, Ted H.
CORPORATE SOURCE: Columbia Sch. Med., Univ. Missouri, Columbia, MO, 65212, USA
SOURCE: J. Exp. Med. (1988), 168(5), 1719-39
CODEN: JEMEAV; ISSN: 0022-1007
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Two phenomena appear to distinguish the D region class I genes from those in the K region in the murine MHC: (a) haplotype disparity in the no. of expressed D region class I mol. has been obstd.; and (b) clines of closely related D region class I mol. among and within mice of different H-2 haplotypes can be defined. Both of these observations have been based on serol. and peptide mapping analyses of these mol. Recent reports using mol. biol. approaches have corroborated these findings. Since the mouse strain B10.AKM expresses multiple D region class I antigens, all of which are closely related to the prototypic Ld mol., the Dq region of B10.AKM was investigated using mol. approaches. Three D region class I genes were isolated from genomic B10.AKM bacteriophage and cosmid libraries. Based on alignment of those genes with the BALB/c D region class I genes by analogous restriction endonuclease sites and by hybridization of one of those genes with a D4d gene-derived oligonucleotide probe, these genes were designated as Dq, Lq, and D4q. As detd. by DNA-mediated gene transfer to mouse L cells followed by serol. analyses, the Dq and Lq genes encode previously characterized Dq region class I antigens. The nucleic acid sequence comparisons of the Dq and Lq genes demonstrated a higher level of homol. with the Ld and Db genes than with other D region class I genes. In addn., CTL stimulated with a Dq, Lq, or Ld gene transfectant showed strong crossreactions with the other transfectants as targets, suggesting that the products of these genes are also functionally related. Thus, these studies suggest that the L mol. represents a prototypic structure shared by several D region gene products, and furthermore, that duplication of an Ld-like progenitor gene resulted in 2 Dq region class I genes, Dq and Lq. Unexpectedly, the sequences detd. for the Dq and Lq genes are nearly identical to the sequences of 2 genes, A166 and A149, resp. which were reported to encode the tumor-specific antigens; these novel class I genes were isolated from an H-2k fibrosarcoma, 1591. This raises the distinct possibility that these purported tumor-specific class I genes were introduced into this tumor by contamination.

L8 ANSWER 16 OF 39 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 97054582 EMBASE
DOCUMENT NUMBER: 1997054582
TITLE: Identification of tyrosinase-related protein 2 as a tumor rejection antigen for the B16 melanoma.
AUTHOR: Bloom M.B.; Perry-Lalley D.; Robbins P.F.; Li Y.; El-Gamil M.; Rosenberg S.A.; Yang J.C.
CORPORATE SOURCE: Dr. J.C. Yang, Surgery Branch, National Cancer Institute, National Institutes of Health, 9000 Rockville Pike, Bethesda, MD 20892, United States
SOURCE: Journal of Experimental Medicine, (1997) 185/3 (453-459).
Refs: 24
ISSN: 0022-1007 **CODEN:** JEMEAV
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 016 Cancer
 026 Immunology, Serology and Transplantation
 037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Recently, major advances have been made in the identification of antigens from human melanoma which are recognized by T cells. In spite of this, little is known about the optimal ways to use these antigens to treat patients with cancer. Progress in this area is likely to require accurate preclinical animal models, but the availability of such models has lagged behind developments in human tumor immunology. Whereas many of the identified human melanoma antigens are normal tissue differentiation proteins, analogous murine tumor antigens have not yet been identified. In this paper we identify a normal tissue differentiation antigen, tyrosinase-related protein 2 (TRP-2), expressed by the murine B16 melanoma which was found by screening a cDNA library from B16 with tumor-reactive cytotoxic T lymphocytes (CTL). A peptide conforming to the predicted MHC class I H2-K^b

binding motif, TRP-2181-188, was identified as the major reactive epitope within TRP-2 recognized by these anti-B16 CTLs. By site-directed mutagenesis, it was shown that alteration of this epitope eliminated recognition of TRP-2. It was further demonstrated that a CTL line raised from splenocytes by repeated stimulation *in vitro* with this peptide could recognize B16 tumor and was therapeutic against 3-d-old established pulmonary metastases. The use of TRP-2 in a preclinical model of tumor immunotherapy may be helpful in suggesting optimal vaccination strategies for cancer therapy in patients.

L8 ANSWER 17 OF 39 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 97028275 EMBASE
DOCUMENT NUMBER: 1997028275
TITLE: Cytotoxic T cell induction with ratchet peptide libraries.
AUTHOR: Kuebler P.J.; Nixon D.F.
CORPORATE SOURCE: D.F. Nixon, Aaron Diamond AIDS Research Center, 455, 1st Avenue, New York, NY 10016, United States
SOURCE: Vaccine, (1996) 14/17-18 (1664-1670).
Refs: 26
ISSN: 0264-410X CODEN: VACCDE
PUBLISHER IDENT.: S 0264-410X(96)00125-9
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
026 Immunology, Serology and Transplantation
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Immunization with synthetic peptides are used to induce cytotoxic T cell (CTL) responses *in vivo*. However, CTL peptide vaccines require the use of multiple peptides to overcome genetic diversity associated with MHC restriction, and prior epitope identification from the chosen protein template. We describe here a method whereby all nonamer sequences from a longer template can be synthesized simultaneously in a ratchet peptide library (RPL) covering all potential epitopes within a protein. We synthesized an RPL based on a template sequence from the Plasmodium berghei circumsporozoite (CS) protein (CSRPL). Using a lipopeptide formulation we immunized mice i.p. with the CSRPL and elicited CS specific CTL, which recognized the CS252-260 H-2K(d) restricted CTL epitope.

L8 ANSWER 18 OF 39 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 97025254 EMBASE
DOCUMENT NUMBER: 1997025254
TITLE: Identification of potential CTL epitopes of bovine RSV using allele-specific peptide motifs from bovine MHC class I molecules.
AUTHOR: Gaddum R.M.; Ellis S.A.; Willis A.C.; Cook R.S.; Staines K.A.; Thomas L.H.; Taylor G.
CORPORATE SOURCE: R.M. Gaddum, Institute for Animal Health, Compton, Newbury RG20 7NN, United Kingdom
SOURCE: Veterinary Immunology and Immunopathology, (1996) 54/1-4 (211-219).
Refs: 50
ISSN: 0165-2427 CODEN: VIIMDS
PUBLISHER IDENT.: S 0165-2427(96)05686-3
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 004 Microbiology
015 Chest Diseases, Thoracic Surgery and Tuberculosis
026 Immunology, Serology and Transplantation
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Respiratory syncytial virus (RSV) is a major cause of lower respiratory tract infection in young infants and housed calves. Depletion of CD8+ lymphocytes from calves inhibited their ability to clear the virus from the nasopharynx and lungs. To study these cells further, a cytotoxic T lymphocyte (CTL) assay was established. CTL could be demonstrated in the peripheral blood of gnotobiotic calves 7-10 days post infection (p.i.) with RSV and in lungs 10 days p.i. This response was both MHC-restricted and virus-specific. Following separation of the lung lymphocytes by magnetic activated cell sorting, it was shown that the cytolytic activity was mediated by cells of the CD8+ phenotype. To identify epitopes recognised by bovine CTL, the consensus motifs from MHC class I alleles found in the herd at Compton were identified. cDNA libraries were constructed and screened for full length class I sequences. The isolated cDNA clones were then transfected into mouse P815 cells and the expressed product immunoprecipitated and matched with a serological specificity. The bovine MHC class I molecules were isolated from lysed transfected cells by affinity chromatography, using a monoclonal antibody specific for bovine MHC class I, and bound peptides were separated by reverse-phase HPLC. Analysis of the protein sequences of bovine RSV for the defined motifs has identified potential CTL epitopes

L8 ANSWER 19 OF 39 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 96225309 EMBASE
DOCUMENT NUMBER: 1996225309
TITLE: Use of combinatorial peptide libraries to construct functional mimics of tumor epitopes recognized by MHC class I-restricted cytolytic T lymphocytes.
AUTHOR: Blake J.; Johnston J.V.; Hellstrom K.E.; Marquardt H.; Chen L.
CORPORATE SOURCE: B.-Myers Squibb Pharma. Res. Inst., 3005 First Avenue, Seattle, WA 98121, United States
SOURCE: Journal of Experimental Medicine, (1996) 184/1 (121-130).
ISSN: 0022-1007 CODEN: JEMEA
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 016 Cancer
026 Immunology, Serology and Transplantation
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Identification of cytolytic T lymphocyte (CTL) epitopes presented by major histocompatibility complex (MHC) class 1 molecules on tumor cells is critical for the design of active

immunotherapy. We describe the rise of combinatorial peptide libraries with defined amino acids in two MHC anchor positions to search for epitopes that are recognized by H-2Db- and Kb-restricted CTL specific for the mouse lymphoma EL4. An iterative strategy was used for screening libraries in which 16 amino acids were divided into 3 groups and 3 subgroups: .alpha.(AL, VT, FY); .beta.(GS, P, DB); .gamma.(KR, H, NQ). The proportions of each group and subgroup at individual peptide positions were changed in the library synthesis, and the effect of these changes on CTL activity was measured in a sensitive RMA-S cell assay. A single H-2Db epitope mimic was deduced from the original library that contained >2 x 10⁸ potential peptides and was at least 9 logs more potent than the original library. Immunization of syngeneic mice with this peptide elicited CTL that lysed EL4 cells as well as RMA-S cells pulsed with peptides isolated from Db molecules of EL4 cells, indicating functional similarity between the mimicking peptide and the naturally processed CTL epitope. Furthermore, adoptive transfer of such a CTL line had a therapeutic effect in mice with EL4 established as an ascites tumor. Two H-2Kb-restricted epitope mimics of the same tumor were also identified. Our method represents a novel approach for the construction of MHC class I-restricted targets that can serve as immunogens for active immunotherapy of cancer.

L8 ANSWER 20 OF 39 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 96211074 EMBASE
 DOCUMENT NUMBER: 1996211074
 TITLE: Self-MHC-restricted peptides recognized by an alloreactive T lymphocyte clone.
 AUTHOR: Ueda K.; Wiesmuller K.-H.; Kienle S.; Jung G.; Walden P.
 CORPORATE SOURCE: Dermatologische Klinik der Charite, Humboldt-Universitat, Schumannstr. 20/21, D-10117 Berlin, Germany
 SOURCE: Journal of Immunology, (1996) 157/2 (670-678).
 ISSN: 0022-1767 CODEN: JOIMAS
 COUNTRY: United States
 DOCUMENT TYPE: Journal; Article
 FILE SEGMENT: 026 Immunology, Serology and Transplantation
 LANGUAGE: English
 SUMMARY LANGUAGE: English
 AB Alloreactive T lymphocytes are readily detected in unprimed animals although they have never encountered the alloantigen before. This well-established phenomenon is usually explained with the assumption that a self-MHC molecule complexed with a defined peptide resembles the allo-MHC molecule with another peptide and induces the corresponding T cell specificities. Here, for the first time and in support of this hypothesis, self-MHC-restricted peptides are described for a T cell clone that was induced with allo-MHC. The allo-MHC-specific CTL clone 2C was derived from a H-2b mouse and recognizes H-2L(d) complexed with the naturally occurring endogenous peptide LSPFPFDL. H-2Kb was shown to be involved in positive selection of its TCR, and peptides associated with this MHC molecule are implicated in the process. To identify such peptides, positional scanning with random peptide libraries combined with an iterative approach was employed. Several active peptides were found and the most efficient, SIYRYYGL, was chosen for further studies. Recognition by 2C of the two MHC-peptide adducts H-2L(d) + LSPFPFDL and H-2K(b) + SIYRYYGL is mediated by the same TCR and appears to be similarly efficient as concluded from inhibition experiments with an Id-specific Ab. CTLs from SIYRYYGL-primed H-2b mice respond to H-2L(d) + LSPFPFDL. This reciprocal cross-reactivity suggests that structural features are shared by the two MHC-peptide complexes.

L8 ANSWER 21 OF 39 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 96144399 EMBASE
 DOCUMENT NUMBER: 1996144399
 TITLE: Specificity and degeneracy of minor histocompatibility antigen-specific MHC-restricted CTL.
 AUTHOR: Gundlach B.R.; Wiesmuller K.-H.; Junt T.; Kienle S.; Jung G.; Walden P.
 CORPORATE SOURCE: Dermatologische Klinik, Humboldt-Universitat, Schumannstr. 20/21, D-10117 Berlin, Germany
 SOURCE: Journal of Immunology, (1996) 156/10 (3645-3651).
 ISSN: 0022-1767 CODEN: JOIMAS
 COUNTRY: United States
 DOCUMENT TYPE: Journal; Article
 FILE SEGMENT: 026 Immunology, Serology and Transplantation
 LANGUAGE: English
 SUMMARY LANGUAGE: English
 AB Random peptide libraries were employed to investigate the specificity of Ag recognition by H-3-specific, H-2Kb-restricted CTL clones. The peptide libraries consist of octapeptides with one defined sequence position and mixtures of 19 amino acids (all proteinogenic amino acids except for cysteine) in the remaining seven sequence positions. The complete set of 152 peptide libraries includes all octapeptides possible with these amino acids. Responses of the CTL clones to these peptide libraries reveal patterns of preferred epitope amino acids. Depending on the CTL clone tested, varying numbers of different amino acids were identified for the different sequence positions indicating degeneracy of Ag recognition. Sequences for synthetic epitopes active at low pM concentrations could be deduced from these patterns. They confirm that TCRs of CTL clones do not exhibit specificity for unique ligand structures but rather can interact with sets of ligands. The sequences of peptides recognized by a single clone exhibit great sequence heterogeneity.

L8 ANSWER 22 OF 39 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 96083797 EMBASE
 DOCUMENT NUMBER: 1996083797
 TITLE: Increased peptide promiscuity provides a rationale for the lack of N regions in the neonatal T cell repertoire.
 AUTHOR: Gavin M.A.; Bevan M.J.
 CORPORATE SOURCE: Department of Immunology, Howard Hughes Medical Institute, University of Washington, Seattle, WA 98195-7370, United States
 SOURCE: Immunity, (1995) 3/6 (793-800).
 ISSN: 1074-7613 CODEN: IUNIEH
 COUNTRY: United States
 DOCUMENT TYPE: Journal; Article
 FILE SEGMENT: 022 Human Genetics

025 Hematology
026 Immunology, Serology and Transplantation
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Making use of mice deficient for terminal deoxynucleotidyl transferase (TdT) expression and a random peptide library, we have examined the diversity and peptide specificity of the neonatal T cell repertoire specific for single H-2D(b)-restricted peptide. Consistent with the predicted decrease in repertoire diversity, polyclonal CTL lines and individual clones from different TdT(o) mice are more similar to each other than those from different wild-type mice in terms of their fingerprints of cross-reactivity to the library and their TCR sequences. We have also found that several TdT(o) CTL clones cross-react with many more library peptides than wild-type CTL clones. In a few instances, the degree of peptide promiscuity correlates with TCR sequence characteristics such as N region addition and homology-directed recombination, but not CDR3 loop length. Based on epitope titrations for each clone, TCR affinity for antigen is consistently high; thus, this reduced specificity for peptide may coincide with an accentuated affinity for the α helices of the MHC. Peptide promiscuity in the neonate may allow the relatively small numbers of T cells in the periphery to protect against a broader range of pathogens.

L8 ANSWER 23 OF 39 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 95169729 EMBASE
DOCUMENT NUMBER: 1995169729
TITLE: Decrypting the structure of major histocompatibility complex class I-restricted cytotoxic T lymphocyte epitopes with complex peptide libraries.
AUTHOR: Udaka K.; Wiesmüller K.-H.; Kienle S.; Jung G.; Walden P.
CORPORATE SOURCE: Max-Planck-Institut für Biologie, Abteilung Immunogenetik, Corrensstrasse 42, D-72076 Tübingen, Germany
SOURCE: Journal of Experimental Medicine, (1995) 181/6 (2097-2108).
ISSN: 0022-1007 CODEN: JEMEAV
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 006 Internal Medicine
026 Immunology, Serology and Transplantation
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Complex synthetic peptide libraries with defined amino acids in one or more positions of the H-2Kb-restricted cytotoxic T lymphocyte (CTL) epitopes SIINFEKL and RGYVYQQL and mixtures of 19 amino acids in the remaining positions were used to analyze the structural requirements of peptide binding to MHC class I molecules and antigen recognition by CTLs. This approach provides means to assess semiquantitatively the contribution of every amino acid to the binding of peptides to major histocompatibility complex (MHC) molecules without biases introduced by naturally processed peptides. Primary and secondary anchor residues were defined for their major contribution to the binding efficiency of the peptides. In contrast to primary anchors, secondary anchor amino acids vary greatly in their side chains and position in the sequences. All amino acids in the octapeptide sequences were found to exhibit positive or negative influences on binding to the MHC molecules and on recognition of the resulting complexes by CTLs. Strong interdependence of the effects of the individual residues in the epitope sequences was demonstrated. CTL responses to peptide libraries were suppressed when residues were introduced; however, they were augmented when the critical residues for T cell recognition were fixed, suggesting a potential use of the peptide libraries for defining epitope sequences in general.

L8 ANSWER 24 OF 39 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 95116981 EMBASE
DOCUMENT NUMBER: 1995116981
TITLE: Isolation of a kidney-specific peptide recognized by alloreactive HLA-A3-restricted human CTL.
AUTHOR: Poindexter N.J.; Naziruddin B.; McCourt D.W.; Mohanakumar T.
CORPORATE SOURCE: Department of Surgery, Washington Univ. School of Medicine, 4939 Children's Place, St. Louis, MO 63110, United States
SOURCE: Journal of Immunology, (1995) 154/8 (3880-3887).
ISSN: 0022-1767 CODEN: JOIMAS
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 026 Immunology, Serology and Transplantation
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The molecular nature of tissue-specific Ags involved in MHC-restricted CTL responses is as yet undefined. To determine the specificity of these peptides, their function, and their possible relationship to allograft rejection, we have utilized human kidney-specific CD8+ CTL clones to screen reversed-phase HPLC (RP-HPLC)-separated self peptides presented by allo-class I molecules. One of these clones is HLA-A3-restricted and the other HLA-B62-restricted, lysing human kidney cell lines but not MHC identical B lymphoblastoid cells which express the appropriate HLA molecules. We have identified a biologically active RP-HPLC fraction containing self peptides eluted from affinity-purified MHC molecules from HLA-A3+ kidney. This peptide is not expressed in HLA-A3+ spleen. Similarly, a HLA-B62-associated peptide fraction was identified in kidney but not in spleen using the HLA-B62-restricted CTL clone. Sequence analysis of the biologically active fraction from HLA-A3 kidney revealed multiple peptides. Because of the ambiguity of the peptide sequence, a mixed peptide library corresponding to this sequence was synthesized that included the HLA-A3 binding motif. The biologically active peptide library was RP-HPLC fractionated and the fraction containing HLA-A3-restricted CTL activity was sequenced. The resulting sequence of the alloreactive HLA-A3-restricted peptide epitope is GPPGVTIVK. By using this unique strategy, we describe the successful isolation and sequencing of an antigenic peptide that is recognized by a human alloreactive kidney-specific CTL clone.

L8 ANSWER 25 OF 39 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 92251943 EMBASE

DOCUMENT NUMBER: 1992251943
TITLE: Influenza basic polymerase 2 peptides are recognized by influenza nucleoprotein-specific cytotoxic T lymphocytes.
AUTHOR: Anderson R.W.; Bennink J.R.; Yewdell J.W.; Maloy W.L.; Coligan J.E.
CORPORATE SOURCE: Biological Resources Branch, NIAID, NIH, Bethesda, MD 20892, United States
SOURCE: Molecular Immunology, (1992) 29/9 (1089-1096).
ISSN: 0161-5890 CODEN: IMCHAZ
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 026 Immunology, Serology and Transplantation
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Cytotoxic T lymphocytes (CTL) play an important role in limiting viral infections and in eradicating virus from host tissues. Recent progress in understanding the processing and presentation of viral antigens to CTL indicates that the CTL antigen receptor recognizes peptides derived from viral proteins that are bound to an antigen binding groove present in class I major histocompatibility complex (MHC) molecules. In understanding CTL anti-viral responses and in creating vaccines designed to elicit CTL responses, it is critical to identify the portions of viral proteins that bind class I molecules and are recognized by T cell receptors. Previous findings have indicated that a significant portion of the CTL response of H-2(d) mice to influenza virus is specific for one of the viral polymerases (PB2). To identify the region of PB2 naturally processed and presented by influenza virus-infected mouse cells to CTL, 31 PB2 peptides of 9-16 residues in length were chosen and chemically synthesized. Two peptides, PB2, residues 146-159 and 187-195, were found to sensitize histocompatible target cells for recognition by influenza virus-specific CTL. When CTL were generated to individual viral proteins using influenza-vaccinia recombinant viruses, we found, to our surprise, that PB2-specific CTL failed to recognize cells sensitized with PB2 peptides 146-159 and 187-195. Further analysis showed that these PB2 peptides were, in fact, recognized by nucleoprotein (NP)-specific CTL generated by NP-vac virus priming and influenza A virus stimulation, or NP peptide stimulation in vitro of NP-vac or influenza A-primed CTL. These results demonstrate that while screening peptide libraries one cannot assume that positive peptides necessarily identify the viral protein to which the CTL response is directed.

L8 ANSWER 26 OF 39 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 91275192 EMBASE
DOCUMENT NUMBER: 1991275192
TITLE: A single amino acid substitution in an MHC class I molecule allows heteroclitic recognition by lymphocytic choriomeningitis virus-specific cytotoxic T lymphocytes.
AUTHOR: Muller D.; Pederson K.; Murray R.; Frelinger J.A.
CORPORATE SOURCE: Microbiology/Immunology Dept., University of North Carolina, Chapel Hill, NC 27599-7290, United States
SOURCE: Journal of Immunology, (1991) 147/4 (1392-1397).
ISSN: 0022-1767 CODEN: JOIMA3
COUNTRY: United States
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 026 Immunology, Serology and Transplantation
047 Virology
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Class I molecules of the MHC bind foreign and endogenous peptides allowing recognition by the TCR on CTL. The recognition and killing of cells infected with lymphocytic choriomeningitis virus (LCMV) depends on the recognition of LCMV peptides bound to class I MHC. Mutations in class I MHC molecules have enabled the delineation of regions in the class I molecule important for binding peptides and for interaction with the TCR. We have constructed a library of class I mutants using saturation mutagenesis and report a phenotypic change resulting from a single amino acid substitution that results in the heteroclitic (increased) killing of LCMV-infected cells. This amino acid change, asparagine to serine at position 30, is in a conserved region of the class I molecule contacting the α .3 domain. This mutation does not result in increased expression of the class I molecule on the cell surface, does not affect the binding of CD8, and does not affect allogeneic recognition. Cold target experiments show that this heteroclitic killing is due to increased recognition by CTL. These data point toward a critical function for this region of the class I molecule in the binding of peptides or their presentation to CTL.

L8 ANSWER 27 OF 39 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 89023259 EMBASE
DOCUMENT NUMBER: 1989023259
TITLE: The murine MHC class I genes, H-2D(q) and H-2L(g), are strikingly homologous to each other, H-2L(d), and two genes reported to encode tumor-specific antigens.
AUTHOR: Lee D.R.; Rubocki R.J.; Lie W.-R.; Hansen T.H.
CORPORATE SOURCE: Department of Microbiology, University of Missouri-Columbia School of Medicine, Columbia, MO 65212, United States
SOURCE: Journal of Experimental Medicine, (1988) 168/5 (1719-1739).
ISSN: 0022-1007 CODEN: JEMEA9
COUNTRY: United States
DOCUMENT TYPE: Journal
FILE SEGMENT: 022 Human Genetics
026 Immunology, Serology and Transplantation
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Two phenomena appear to distinguish the D region class I genes from those in the K region in the murine MHC: (a) haplotype disparity in the number of expressed D region class I molecules has been observed; and (b) clines of closely related D region class I molecules among and within mice of different H-2 haplotypes can be defined. Both of these observations have been based on serological and peptide mapping analyses of these molecules. Recent reports using molecular biological approaches have corroborated these findings. Since the mouse strain B10.AKM expresses multiple D region class I antigens, all of which are closely related to the prototypic L(d) molecule, we investigated the D(q) region of B10.AKM using molecular approaches. Three D region class I genes were isolated from genomic B10.AKM bacteriophage and cosmid

libraries. Based on alignment of those genes with the BALB/c D region class I genes by analogous restriction endonuclease sites and by hybridization of one of those genes with a D_{4(d)} gene-derived oligonucleotide probe, we have designated these genes as D(q), L(q), and D_{4(q)}. As determined by DNA mediated gene transfer to mouse L cells followed by serological analyses, the D(q) and L(q) genes encode previously characterized D(q) region class I antigens. The nucleic acid sequence comparisons of the D(q) and L(q) genes demonstrated a higher level of homology with the L(d) and Db genes than with other D region class I genes. In addition, CTL stimulated with a D(q), L(q), or L(d) gene transfectant showed strong crossreactions with the other transfectants as targets, suggesting that the products of these genes are also functionally related. Thus, these studies suggest that the L molecule represents a prototypic structure shared by several D region gene products, and furthermore, that duplication of an L(d)-like progenitor gene resulted in two D(q) region class I genes, D(q) and L(q). Unexpectedly, the sequences determined for the D(q) and L(q) genes are nearly identical to the sequences of two genes, A166 and A149, respectively, which were reported to encode the tumor-specific antigens; these novel class I genes were isolated from an H-2(k) fibrosarcoma, 1591. This raises the distinct possibility that these purported tumor-specific class I genes were introduced into this tumor by contamination.

L8 ANSWER 28 OF 39 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 1997:386470 BIOSIS
DOCUMENT NUMBER: PREV199799685673
TITLE: Antigen processing by proteasomes: Insights into the molecular basis of crypticity.
AUTHOR(S): Djaballah, Hakim
CORPORATE SOURCE: MRC Transplantation Biol. Group, Royal Postgrad. Med. Sch., Hammersmith Hosp., Du Cane Road, London W12 0NN UK
SOURCE: Molecular Biology Reports, (1997) Vol. 24, No. 1-2, pp. 63-67.
ISSN: 0301-4851.

DOCUMENT TYPE: General Review

LANGUAGE: English

AB Eight to eleven amino acid residues are the sizes of predominant peptides found to be associated with MHC class I molecules. Proteasomes have been implicated in antigen processing and generation of such peptides. Advanced methodologies in peptide elution together with sequence determination have led to the characterization of MHC class I binding motifs. More recently, screening of random peptide phage display libraries and synthetic combinatorial peptide libraries have also been successfully used. This has led to the development and use of predictive algorithms to screen antigens for potential CTL epitopes. Not all predicted epitopes will be generated in vivo and the emerging picture suggests differential presentation of predicted CTL epitopes ranging from cryptic to immunodominant. The scope of this review is to discuss antigen processing by proteasomes, and to put forward a hypothesis that the molecular basis of immunogenicity can be a function of proteasomal processing. This may explain how pathogens and tumours are able to escape immunosurveillance by altering sequences required by proteasomes for epitope generation.

L8 ANSWER 29 OF 39 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 1997:119732 BIOSIS
DOCUMENT NUMBER: PREV199799426235
TITLE: Identification of tyrosinase-related protein 2 as a tumor rejection antigen for the B16 melanoma.
AUTHOR(S): Bloom, Matthew B.; Perry-Lalley, Donna; Robbins, Paul F.; Li, Yong; El-Gamil, Mona; Rosenberg, Steven A.; Yang, James C.
CORPORATE SOURCE: Surg. Branch, National Cancer Inst., National Inst. Health, Bethesda, MD 20892 USA
SOURCE: Journal of Experimental Medicine, (1997) Vol. 185, No. 3, pp. 453-459.
ISSN: 0022-1007.

DOCUMENT TYPE: Article

LANGUAGE: English

AB Recently, major advances have been made in the identification of antigens from human melanoma which are recognized by T cells. In spite of this, little is known about the optimal ways to use these antigens to treat patients with cancer. Progress in this area is likely to require accurate preclinical animal models, but the availability of such models has lagged behind developments in human tumor immunology. Whereas many of the identified human melanoma antigens are normal tissue differentiation proteins, analogous murine tumor antigens have not yet been identified. In this paper we identify a normal tissue differentiation antigen, tyrosinase-related protein 2 (TRP-2), expressed by the murine B16 melanoma which was found by screening a cDNA library from B16 with tumor-reactive cytotoxic T lymphocytes (CTL). A peptide conforming to the predicted MHC class I H2-K_b binding motif, TRP-2-181-188, was identified as the major reactive epitope within TRP-2 recognized by these anti-B16 CTLs. By site-directed mutagenesis, it was shown that alteration of this epitope eliminated recognition of TRP-2. It was further demonstrated that a CTL line raised from splenocytes by repeated stimulation in vitro with this peptide could recognize B16 tumor and was therapeutic against 3-d-old established pulmonary metastases. The use of TRP-2 in a preclinical model of tumor immunotherapy may be helpful in suggesting optimal vaccination strategies for cancer therapy in patients.

L8 ANSWER 30 OF 39 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 1997:111284 BIOSIS
DOCUMENT NUMBER: PREV199799410487
TITLE: Cytotoxic T cell induction with ratchet peptide libraries.
AUTHOR(S): Kuebler, Peter J.; Nixon, Douglas F. (1)
CORPORATE SOURCE: (1) Aaron Diamond AIDS Res. Cent., 455, 1st Avenue, New York, NY 10016 USA
SOURCE: Vaccine, (1996) Vol. 14, No. 17-18, pp. 1664-1670.
ISSN: 0264-410X.

DOCUMENT TYPE: Article

LANGUAGE: English

AB Immunization with synthetic peptides are used to induce cytotoxic T cell (CTL) responses in vivo. However, CTL peptide vaccines require the use of multiple peptides to overcome genetic diversity associated with MHC restriction, and prior epitope identification from the chosen protein template. We describe here a method whereby all nonamer sequences from a longer

template can be synthesized simultaneously in a ratchet peptide library (RPL) covering all potential epitopes within a protein. We synthesized an RPL based on a template sequence from the Plasmodium berghei circumsporozoite (CS) protein (CSRPL). Using a lipopeptide formulation we immunized mice i. p. with the CSRPL and elicited CS specific CTL, which recognized the CS252-260 H-2K-d restricted CTL epitope.

L8 ANSWER 31 OF 39 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 1996:383101 BIOSIS

DOCUMENT NUMBER: PREV199699105457

TITLE: Use of combinatorial peptide libraries to construct functional mimics of tumor epitopes recognized by MHC class I-restricted cytolytic T lymphocytes.

AUTHOR(S): Blake, James; Johnston, Janet V.; Hellstrom, Karl Erik; Marquardt, Hans; Chen, Lieping (1)

CORPORATE SOURCE: (1) Bristol-Myers Squibb Pharmaceutical Res. Inst., 3005 First Ave., Seattle, WA 98121 USA

SOURCE: Journal of Experimental Medicine, (1996) Vol. 184, No. 1, pp. 121-130.

ISSN: 0022-1007.

DOCUMENT TYPE: Article

LANGUAGE: English

AB Identification of cytolytic T lymphocyte (CTL) epitopes presented by major histocompatibility complex (MHC) class I molecules on tumor cells is critical for the design of active immunotherapy. We describe the use of combinatorial peptide libraries with defined amino acids in two MHC anchor positions to search for epitopes that are recognized by H-2D-b- and K-b- restricted CTL specific for the mouse lymphoma EL4. An iterative strategy was used for screening libraries in which 16 amino acids were divided into 3 groups and 3 subgroups: alpha(AL, VT, FY); beta(GS, P, DE); gamma(KR, H, NQ). The proportions of each group and subgroup at individual peptide positions were changed in the library synthesis, and the effect of these changes on CTL activity was measured in a sensitive RMA-S cell assay. A single H-2D-b epitope mimic was deduced from the original library that contained gt 2 times 10-8 potential peptides and was at least 9 logs more potent than the original library. Immunization of syngeneic mice with this peptide elicited CTL that lysed EL4 cells as well as RMA-S cells pulsed with peptides isolated from D-b molecules of EL4 cells, indicating functional similarity between the mimicking peptide and the naturally processed CTL epitope. Furthermore, adoptive transfer of such a CTL line had a therapeutic effect in mice with EL4 established as an ascites tumor. Two H-2K-b-restricted epitope mimics of the same tumor were also identified. Our method represents a novel approach for the construction of MHC class I-restricted targets that can serve as immunogens for active immunotherapy of cancer.

L8 ANSWER 32 OF 39 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 1996:381263 BIOSIS

DOCUMENT NUMBER: PREV199699103619

TITLE: Self-MHC-restricted peptides recognized by an alloreactive T lymphocyte clone.

AUTHOR(S): Ueda, Keiko; Wiesmueller, Karl-Heinz; Kienle, Stefan; Jung, Guenther; Walden, Peter (1)

CORPORATE SOURCE: (1) Dermatologische Klinik der Charite, Humboldt-Univ., Schumannstr. 20/21, D-10117 Berlin Germany

SOURCE: Journal of Immunology, (1996) Vol. 157, No. 2, pp. 670-678.

ISSN: 0022-1767.

DOCUMENT TYPE: Article

LANGUAGE: English

AB Alloreactive T lymphocytes are readily detected in unprimed animals although they have never encountered the alioantigen before. This well-established phenomenon is usually explained with the assumption that a self-MHC molecule complexed with a defined peptide resembles the allo-MHC molecule with another peptide and induces the corresponding T cell specificities. Here, for the first time and in support of this hypothesis, self-MHC-restricted peptides are described for a T cell clone that was induced with allo-MHC. The allo-MHC-specific CTL clone 2C was derived from a H-2-b mouse and recognizes H-2L-d complexed with the naturally occurring endogenous peptide LSPPPFDL. H-2K-b was shown to be involved in positive selection of its TCR, and peptides associated with this MHC molecule are implicated in the process. To identify such peptides, positional scanning with random peptide libraries combined with an iterative approach was employed. Several active peptides were found and the most efficient, SIYRYYGL, was chosen for further studies. Recognition by 2C of the two MHC-peptide adducts H-2L-d+ LSPPPFDL and H-2K-b + SIYRYYGL is mediated by the same TCR and appears to be similarly efficient as concluded from inhibition experiments with an Id-specific Ab. CTLs from SIYRYYGL-primed H-2-b mice respond to H-2L-d + LSPPPFDL. This reciprocal cross-reactivity suggests that structural features are shared by the two MHC-peptide complexes.

L8 ANSWER 33 OF 39 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 1996:284018 BIOSIS

DOCUMENT NUMBER: PREV199699006374

TITLE: Specificity and degeneracy of minor histocompatibility antigen-specific MHC-restricted CTL.

AUTHOR(S): Gundlach, Bjorn R.; Wiesmueller, Karl-Heinz; Junt, Tobias; Kienle, Stefan; Jung, Guenther; Walden, Peter (1)

CORPORATE SOURCE: (1) Dermatol. Klinik, Charite, Humboldt-Universitaet, Schumannstr. 20/21, D-10117 Berlin Germany

SOURCE: Journal of Immunology, (1996) Vol. 156, No. 10, pp. 3645-3651.

ISSN: 0022-1767.

DOCUMENT TYPE: Article

LANGUAGE: English

AB Random peptide libraries were employed to investigate the specificity of Ag recognition by H-3-specific, H-2K-b-restricted CTL clones. The peptide libraries consist of octapeptides with one defined sequence position and mixtures of 19 amino acids (all proteinogenic amino acids except for cysteine) in the remaining seven sequence positions. The complete set of 152 peptide libraries includes all octapeptides possible with these amino acids. Responses of the CTL clones to these peptide libraries reveal patterns of preferred epitope amino

acids. Depending on the CTL clone tested, varying numbers of different amino acids were identified for the different sequence positions indicating degeneracy of Ag recognition. Sequences for synthetic epitopes active at low pM concentrations could be deduced from these patterns. They confirm that TCRs of CTL clones do not exhibit specificity for unique ligand structures but rather can interact with sets of ligands. The sequences of peptides recognized by a single clone exhibit great sequence heterogeneity.

L8 ANSWER 34 OF 39 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 1995:309438 BIOSIS

DOCUMENT NUMBER: PREV199598323738

TITLE: Decrypting the Structure of Major Histocompatibility Complex Class I-Restricted Cytotoxic T Lymphocytes

Epitopes with Complex Peptide Libraries.

AUTHOR(S): Ueda, Keiko; Wiesmueller, Karl-Heinz; Kienle, Stefan;

Jung, Guenther; Walden, Peter (1)

CORPORATE SOURCE: (1) Max Planck Inst. Biol., Abteilung Immunogenet.,

Corrensstrasse 42, D-72076 Tuebingen Germany

SOURCE: Journal of Experimental Medicine, (1995) Vol. 181, No. 6, pp. 2097-2108.

ISSN: 0022-1007.

DOCUMENT TYPE: Article

LANGUAGE: English

AB Complex synthetic peptide libraries with defined amino acids in one or more positions of the H-2K-b-restricted cytotoxic T lymphocyte (CTL) epitopes S1INFEKL and RGYVYQGL and mixtures of 19 amino acids in the remaining positions were used to analyze the structural requirements of peptide binding to MHC class I molecules and antigen recognition by CTLs. This approach provides means to assess semiquantitatively the contribution of every amino acid to the binding of peptides to major histocompatibility complex (MHC) molecules without biases introduced by naturally processed peptides. Primary and secondary anchor residues were defined for their major contribution to the binding efficiency of the peptides. In contrast to primary anchors, secondary anchor amino acids vary greatly in their side chains and position in the sequences. All amino acids in the octapeptide sequences were found to exhibit positive or negative influences on binding to the MHC molecules and on recognition of the resulting complexes by CTLs. Strong interdependence of the effects of the individual residues in the epitope sequences was demonstrated. CTL responses to peptide libraries were suppressed when residues were introduced; however, they were augmented when the critical residues for T cell recognition were fixed, suggesting a potential use of the peptide libraries for defining epitope sequences in general.

L8 ANSWER 35 OF 39 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 1995:221511 BIOSIS

DOCUMENT NUMBER: PREV199598235811

TITLE: Isolation of a kidney-specific peptide recognized by alloreactive HLA-A3-restricted human CTL.

AUTHOR(S): Poindexter, Nancy J.; Naziruddin, Bashoo; McCourt, David W.; Mohanakumar, T. (1)

CORPORATE SOURCE: (1) Dep. Surgery, P.O. Box 8109-CSRB 4449, Washington Univ. Sch. Med., 4939 Children's Place, St. Louis, MO 63110 USA

SOURCE: Journal of Immunology, (1995) Vol. 154, No. 8, pp. 3880-3887.

ISSN: 0022-1767.

DOCUMENT TYPE: Article

LANGUAGE: English

AB The molecular nature of tissue-specific Ags involved in MHC-restricted CTL responses is as yet undefined. To determine the specificity of these peptides, their function, and their possible relationship to allograft rejection, we have utilized human kidney-specific CD8+ CTL clones to screen reversed-phase HPLC (RP-HPLC)-separated self peptides presented by allo-class I molecules. One of these clones is HLA-A3-restricted and the other HLA-B62-restricted, lysing human kidney cell lines but not MHC identical B lymphoblastoid cells which express the appropriate HLA molecules. We have identified a biologically active RP-HPLC fraction containing self peptides eluted from affinity-purified MHC molecules from HLA-A3+ kidney. This peptide is not expressed in HLA-A3+ spleen. Similarly, a HLA-B62-associated peptide fraction was identified in kidney but not in spleen using the HLA-B62-restricted CTL clone. Sequence analysis of the biologically active fraction from HLA-A3 kidney revealed multiple peptides. Because of the ambiguity of the peptide sequence, a mixed peptide library corresponding to this sequence was synthesized that included the HLA-A3 binding motif. The biologically active peptide library was RP-HPLC fractionated and the fraction containing HLA-A3-restricted CTL activity was sequenced. The resulting sequence of the alloreactive HLA-A3-restricted peptide epitope is GPPGVIVK. By using this unique strategy, we describe the successful isolation and sequencing of an antigenic peptide that is recognized by a human alloreactive kidney-specific CTL clone.

L8 ANSWER 36 OF 39 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 1994:406226 BIOSIS

DOCUMENT NUMBER: PREV199497419226

TITLE: Class I MHC-peptide interaction:

Structural and functional aspects.

AUTHOR(S): Ruppert, J.; Kubo, R. T.; Sidney, J.; Grey, H. M.; Sette, A.

CORPORATE SOURCE: Cytel, 3525 John Hopkins Court, San Diego, CA 92121 USA

SOURCE: Behring Institute Mitteilungen, (1994) Vol. 0, No. 94, pp. 48-60.

ISSN: 0301-0457.

DOCUMENT TYPE: Article

LANGUAGE: English

AB The structural requirements for the interaction between antigens and class I molecules was investigated through the use of a quantitative assay to measure peptide binding to different MHC class I alleles. We determined the permissiveness of the main anchors reported by Rammensee and his group for peptide binding and defined an extended motif for peptides binding to the HLA-A2.1 allele, including the role of non-anchor positions. It was found that the main anchors were necessary, but not sufficient, for good binding. Certain non-anchor positions contributed significantly to overall binding and were referred to as secondary anchors. This finding allowed a better prediction

of high affinity binding peptides selected from libraries of different viral and tumor proteins. Furthermore, our data allowed correlation of the structural requirements for binding of peptides with crystallographic data of the MHC molecule. In order to characterize allele-specific motifs for a larger number of alleles, the HLA-A alleles A1, A3, A11, and A24, which represent some of the most common alleles found in different ethnic populations, were chosen. Here, most motifs were found to be highly exclusive; however, HLA-A3 and A11 shared a common motif. The defined motifs were validated further by using naturally processed peptides. Those peptides were also synthesized and tested for binding to the appropriate HLA alleles, giving a binding affinity from 0.3 to 200 nM for sequences of naturally processed peptides. Finally, a set of all possible 9-mer peptides from HPV 16 proteins were synthesized and tested for binding to the five class I alleles. For each allele, high affinity binders were identified, thus allowing for selection of possible peptide candidates for a CTL based vaccine.

L8 ANSWER 37 OF 39 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 1992:477182 BIOSIS

DOCUMENT NUMBER: BA94:108557

TITLE: INFLUENZA BASIC POLYMERASE 2 PEPTIDES ARE RECOGNIZED BY INFLUENZA NUCLEOPROTEIN-SPECIFIC CYTOTOXIC T LYMPHOCYTES.

AUTHOR(S): ANDERSON R W; BENNINK J R; YEWDELL J W; MALOY W L; COLIGAN J E

CORPORATE SOURCE: BIOLOGICAL RESOURCES BRANCH, NIAID, NIH, BUILD., 4, ROOM 413, BETHESDA, MD. 20892.

SOURCE: MOL IMMUNOL, (1992) 29 (9), 1089-1096.
CODEN: MOIMD5. ISSN: 0161-5890.

FILE SEGMENT: BA; OLD

LANGUAGE: English

AB Cytotoxic T lymphocytes (CTL) play an important role in limiting viral infections and in eradicating virus from host tissues. Recent progress in understanding the processing and presentation of viral antigens to CTL indicates that the CTL antigen receptor recognizes peptides derived from viral proteins that are bound to an antigen binding groove present in class I major histocompatibility complex (MHC) molecules. In understanding CTL anti-viral responses and in creating vaccines designed to elicit CTL responses, it is critical to identify the portions of viral proteins that bind class I molecules and are recognized by T cell receptors. Previous findings have indicated that a significant portion of the CTL response of H-2d mice to influenza virus is specific for one of the viral polymerases (PB2). To identify the region of PB2 naturally processed and presented by influenza virus-infected mouse cells to CTL, 31 PB2 peptides of 9-16 residues in length were chosen and chemically synthesized. Two peptides, PB2, residues 146-159 and 187-195, were found to sensitize histocompatible target cells for recognition by influenza virus-specific CTL. When CTL were generated to individual viral proteins using influenza-vaccinia recombinant viruses, we found, to our surprise, that PB2-specific CTL failed to recognize cells sensitized with PB2 peptides 146-159 and 187-195. Further analysis showed that these PB2 peptides were, in fact, recognized by nucleoprotein (NP)-specific CTL generated by NP-vac virus priming and influenza A virus stimulation, or NP peptide stimulation in vitro of NP-vac or influenza A-primed CTL. These results demonstrate that while screening peptide libraries one cannot assume that positive peptides necessarily identify the viral protein to which the CTL response is directed.

L8 ANSWER 38 OF 39 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 1991:455244 BIOSIS

DOCUMENT NUMBER: BA92:100024

TITLE: A SINGLE AMINO ACID SUBSTITUTION IN AN MHC CLASS I MOLECULE ALLOWS HETEROCLITIC RECOGNITION BY LYMPHOCYTIC CHORIO MENINGITIS VIRUS-SPECIFIC CYTOTOXIC T LYMPHOCYTES.

AUTHOR(S): MULLER D; PEDERSON K; MURRAY R; FRELINGER J A
CORPORATE SOURCE: DEP. MICROBIOL. IMMUNOL. UNIV. NORTH CAROLINA, CHAPEL HILL, N.C. 27599-7290.

SOURCE: J IMMUNOL, (1991) 147 (4), 1392-1397.
CODEN: JOIMAJ. ISSN: 0022-1767.

FILE SEGMENT: BA; OLD

LANGUAGE: English

AB Class I molecules of the MHC bind foreign and endogenous peptides allowing recognition by the TCR on CTL. The recognition and killing of cells infected with lymphocytic choriomeningitis virus (LCMV) depends on the recognition of LCMV peptides bound to class I MHC. Mutations in class I MHC molecules have enabled the delineation of regions in the class I molecule important for binding peptides and for interaction with the TCR. We have constructed a library of class I mutants using saturation mutagenesis and report a phenotypic change resulting from a single amino acid substitution that results in the heteroclitic (increased) killing of LCMV-infected cells. This amino acid change, asparagine to serine at position 30, is in a conserved region of the class I molecule contacting the alpha₃ domain. This mutation does not result in increased expression of the class I molecule on the cell surface, does not affect the binding of CD8, and does not affect allogeneic recognition. Cold target experiments show that this heteroclitic killing is due to increased recognition by CTL. These data point toward a critical function for this region of the class I molecule in the binding of peptides or their presentation to CTL.

L8 ANSWER 39 OF 39 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 1989:75020 BIOSIS

DOCUMENT NUMBER: BA87:39418

TITLE: THE MURINE MHC CLASS I GENES H-2D-Q AND H-2L-Q ARE STRIKINGLY HOMOLOGOUS TO EACH OTHER H-2L-D AND TWO GENES REPORTED TO ENCODE TUMOR-SPECIFIC ANTIGENS.

AUTHOR(S): LEE D R; RUBOCKI R J; LIE W-R; HANSEN T H
CORPORATE SOURCE: DEP. MICROBIOL., UNIV. MO.-COLUMBIA SCH. MED., COLUMBIA, MO. 65212.

SOURCE: J EXP MED, (1988) 168 (5), 1719-1740.
CODEN: JEMEAV. ISSN: 0022-1007.

FILE SEGMENT: BA; OLD

LANGUAGE: English

AB Two phenomena appear to distinguish the D region class I genes from those in the K region in the murine MHC: (a) haplotype disparity in the number of expressed D region class I molecules has been observed; and (b) clines of closely related D region class I molecules among and within

mice of different H-2 haplotypes can be defined. Both of these observations have been based on serological and peptide mapping analyses of these molecules. Recent reports using molecular biological approaches have corroborated these findings. Since the mouse strain B10.AKM expresses multiple D region class I antigens, all of which are closely related to the prototypic Ld molecule, we investigated the Dq region of B10.AKM using molecular approaches. Three D region class I genes were isolated from genomic B10.AKM bacteriophage and cosmid libraries. Based on alignment of those genes with the BALB/c D region class I genes by analogous restriction endonuclease sites and by hybridization of one of those genes with a Dd gene-derived oligonucleotide probe, we have designated these genes as Dq, Lq, and D4q. As determined by DNA-mediated gene transfer to mouse L cells followed by serological analyses, the Dq and Lq genes encode previously characterized Dq region class I antigens. The nucleic acid sequence comparisons of the Dq and Lq genes demonstrated a higher level of homology with the Ld and Db genes than with other D region class I genes. In addition, CTL stimulated with a Dq, Lq, or Ld gene transfectant showed strong crossreactions with the other transfectants as targets, suggesting that the products of these genes are also functionally related. Thus, these studies suggest that the L molecule represents a prototypic structure shared by several D region gene products, and furthermore, that duplication of an Ld-like progenitor gene resulted in two Dq region class I genes, Dq and Lq. Unexpectedly, the sequences determined for the Dq and Lq genes are nearly identical to the sequences of two genes, A166 and A149, respectively, which were reported to encode the tumor-specific antigens; these novel class I genes were isolated from an H-2^k fibrosarcoma, 1591. This raises the distinct possibility that these purported tumor-specific class I genes were introduced into this tumor by contamination.

=> dis his

(FILE 'HOME' ENTERED AT 07:13:43 ON 03 JUN 2002)

FILE 'MEDLINE, CAPLUS, EMBASE, BIOSIS' ENTERED AT 07:13:57 ON 03 JUN 2002
 L1 127 S ZAUDERER M/AU
 L2 4 S L1 AND CTL?
 L3 4 DUP REM L2 (0 DUPLICATES REMOVED)
 L4 192122 S LIBRAR?
 L5 366 S L4 (P) CTL
 L6 146 S L5 AND PD<19970922
 L7 89 S L6 (P) (EPITOP? OR PEPTID?)
 L8 39 S L7 AND MHC

=> s 18 and (poxvirus or vaccinia)
 L9 3 L8 AND (POXVIRUS OR VACCINIA)

=> dis 18 1-2 ibib abs

L8 ANSWER 1 OF 39 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1997:462415 CAPLUS
 DOCUMENT NUMBER: 127:189254
 TITLE: Antigen processing by proteasomes: insights into the molecular basis of crypticity
 AUTHOR(S): Djaballah, Hakim
 CORPORATE SOURCE: MRC Transplantation Biology Group, Royal Postgraduate Medical School, Hammersmith Hospital, London, W12 0NN, UK
 SOURCE: Mol. Biol. Rep. (1997), 24(1-2), 63-67
 CODEN: MLRBU; ISSN: 0301-4851
 PUBLISHER: Kluwer
 DOCUMENT TYPE: Journal; General Review
 LANGUAGE: English

AB A review with 44 refs. Eight to eleven amino acid residues are the sizes of predominant peptides found to be assoccd. with MHC class I molc. Proteasomes have been implicated in antigen processing and generation of such peptides. Advanced methodologies in peptide elution together with sequence detn. have led to the characterization of MHC class I binding motifs. More recently, screening of random peptide phage display libraries and synthetic combinatorial peptide libraries have also been successfully used. This has led to the development and use of predictive algorithms to screen antigens for potential cytotoxic T-lymphocyte (CTL) epitopes. Not all predicted epitopes will be generated in vivo and the emerging picture suggests differential presentation of predicted CTL epitopes ranging from cryptic to immunodominant. Antigen processing by proteasomes is discussed, a hypothesis that the mol. basis of immunogenicity can be a function of proteasomal processing is advanced. This may explain how pathogens and tumors are able to escape immunosurveillance by altering sequences required by proteasomes for epitope generation.

L8 ANSWER 2 OF 39 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1997:147340 CAPLUS
 DOCUMENT NUMBER: 126:198410
 TITLE: Cytotoxic T cell induction with ratchet peptide libraries
 AUTHOR(S): Kuebler, Peter J.; Nixon, Douglas F.
 CORPORATE SOURCE: United Biomedical, Inc., Hauppauge, NY, 11788, USA
 SOURCE: Vaccine (1996), 14(17/18), 1664-1670
 CODEN: VACCD; ISSN: 0264-410X
 PUBLISHER: Elsevier
 DOCUMENT TYPE: Journal
 LANGUAGE: English

AB Immunization with synthetic peptides are used to induce cytotoxic T cell (CTL) responses in vivo. However, CTL peptide vaccines require the use of multiple peptides to overcome genetic diversity assoccd. with MHC restriction, and prior epitope identification from the chosen protein template. The authors describe here a method whereby all nonamer sequences from a longer template can be synthesized simultaneously in a ratchet peptide library (RPL) covering all potential epitopes within a protein. The authors synthesized an RPL based on a template sequence from the Plasmodium berghei circumsporozoite (CS) protein (CSRPL). Using a lipopeptide formulation the authors immunized mice i.p. with the CSRPL and elicited CS specific CTL, which recognized the CS252-260 H-2Kd restricted CTL epitope.

-> dis 18 3 ibib abs

L8 ANSWER 3 OF 39 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:111450 CAPLUS
DOCUMENT NUMBER: 126:184804
TITLE: Identification of tyrosinase-related protein 2 as a tumor rejection antigen for the B16 melanoma
AUTHOR(S): bloom, Matthew B.; Perry-Lalley, Donna; Robbins, Paul F.; Li, Yong; El-Gamil, Mona; Rosenberg, Steven A.; Yang, James C.
CORPORATE SOURCE: Natl. Cancer Inst., Natl. Inst. Health, Bethesda, MD, 20892, USA
SOURCE: J. Exp. Med. (1997), 185(3), 453-459
CODEN: JEMEAV; ISSN: 0022-1007
PUBLISHER: Rockefeller University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Recently, major advances have been made in the identification of antigens from human melanoma which are recognized by T cells. In spite of this, little is known about the optimal ways to use these antigens to treat patients with cancer. Progress in this area is likely to require accurate preclin. animal models, but the availability of such models has lagged behind developments in human tumor immunol. Whereas many of the identified human melanoma antigens are normal tissue differentiation proteins, analogous murine tumor antigens have not yet been identified. In this paper we identify a normal tissue differentiation antigen, tyrosinase-related protein 2 (TRP-2), expressed by the murine B16 melanoma which was found by screening a cDNA library from B16 with tumor-reactive cytotoxic T lymphocytes (CTL). A peptide conforming to the predicted MHC class I H2-K^b binding motif, TRP-2181-188, was identified as the major reactive epitope within TRP-2 recognized by these anti-B16 CTLs. By site-directed mutagenesis, it was shown that alteration of this epitope eliminated recognition of TRP-2. It was further demonstrated that the CTL line obtained from splenocytes by repeated stimulation in vitro with this peptide could recognize B16 tumor and was therapeutic against 3-d-old established pulmonary metastases. The use of TRP-2 in a preclin. model of tumor immunotherapy may be helpful in suggesting optimal vaccination strategies for cancer therapy in patients.

-> dis his

(FILE 'HOME' ENTERED AT 07:13:43 ON 03 JUN 2002)
FILE 'MEDLINE, CAPLUS, EMBASE, BIOSIS' ENTERED AT 07:13:57 ON 03 JUN 2002
L1 127 S ZAUDERER M/AU
L2 4 S L1 AND CTL?
L3 4 DUP REM L2 (0 DUPLICATES REMOVED)
L4 192122 S LIBRAR?
L5 366 S L4 (P) CTL
L6 146 S L5 AND PD<19970922
L7 89 S L6 (P) (EPITOP? OR PEPTID?)
L8 39 S L7 AND MHC
L9 3 S L8 AND (POXVIRUS OR VACCINIA)

=> s l7 and helper
L10 0 L7 AND HELPER

=> s l7 and tk
L11 0 L7 AND TK

=> s l7 and thymidine
L12 0 L7 AND THYMIDINE

=> s l7 and kinase
L13 0 L7 AND KINASE

=> s v7.5/tk
'TK' IS NOT A VALID FIELD CODE
L14 0 V7.5/TK

=> s v7.5 (1N) tk
L15 0 V7.5 (1N) TK

=> s l7 and homologous
L16 12 L7 AND HOMOLOGOUS

=> s l7 and (homologous (1N) recombination)
L17 0 L7 AND (HOMOLOGOUS (1N) RECOMBINATION)

=> s l7 and transfer (1N) plasmid)
UNMATCHED RIGHT PARENTHESIS 'PLASMID'
The number of right parentheses in a query must be equal to the number of left parentheses.

=> s l7 and (transfer (1N) plasmid)
L18 0 L7 AND (TRANSFER (1N) PLASMID)

=> s (transfer (1N) plasmid)
L19 5607 (TRANSFER (1N) PLASMID)

-> dis his

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FILE 'MEDLINE, CAPLUS, EMBASE, BIOSIS' ENTERED AT 07:13:57 ON 03 JUN 2002
L1 127 S ZAUDERER M/AU
L2 4 S L1 AND CTL?
L3 4 DUP REM L2 (0 DUPLICATES REMOVED)
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L5 366 S L4 (P) CTL
L6 146 S L5 AND PD<19970922
L7 89 S L6 (P) (EPITOP? OR PEPTID?)
L8 39 S L7 AND MHC
L9 3 S L8 AND (POXVIRUS OR VACCINIA)
L10 0 S L7 AND HELPER
L11 0 S L7 AND TK
L12 0 S L7 AND THYMIDINE

L13 0 S L7 AND KINASE
L14 0 S V7.5/TK
L15 0 S V7.5 (1N) TK
L16 12 S L7 AND HOMOLOGOUS
L17 0 S L7 AND (HOMOLOGOUS (1N) RECOMBINATION)
L18 0 S L7 AND (TRANSFER (1N) PLASMID)
L19 5607 S (TRANSFER (1N) PLASMID)

=> end
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LOGOFF? (Y)/N/HOLD:y

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